

Hot Topic: Keep The Head Cool

by Peter Safar, M.D.

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Since the 1970s, many drug therapy trials for cerebral resuscitation after cardiac arrest have yielded results without clear-cut benefits, except those of hypertensive reperfusion and brain-oriented general intensive care. Since 1987, a chance discovery and subsequent systematic studies at the International Resuscitation Research Center (IRRC) have documented that mild brain cooling may be good for the brain without hurting the heart.

Moderate Hypothermia (30° C)

Since the 1950s, cerebral protection by moderate hypothermia induced before elective circulatory arrest has been established and in use for open-heart surgery and neurosurgery.¹ Cerebral resuscitation by moderate hypothermia induced after cardiac arrest, although tried in uncontrolled studies in the 1950s by others, and used empirically on patients by others as well as by us, was not researched. Interest in hypothermia faded because of cardiovascular side effects and management problems. Since 1970, we have had resuscitative hypothermia on our list of brain resuscitation potentials in need of study.

In the early 1980s, IRRC fellow Gisvold conducted a study of a combination treatment, including moderate hypothermia, using our monkey neck tourniquet model, which was developed in the 1970s by Nemoto, et al. The results of this study showed only a suggestive benefit.² In 1987, we conducted the first controlled,

outcome study of moderate resuscitative hypothermia after prolonged cardiac arrest, using our reproducible dog model.³ After 17 minutes of ventricular fibrillation (no flow) at normothermia, total body cooling was achieved with cardiopulmonary bypass from reperfusion to two hours.

Hypothermia caused no significant improvement in functional outcome, a significant improvement in brain histopathologic damage scores, and worsening of heart morphologic damage scores. We speculated that the potential beneficial effect of moderate hypothermia at the neuronal level might not be revealed after such a severe insult, or might be offset by deleterious effects on the heart and cerebral microcirculation. Indeed, we did multifocal cerebral blood flow studies using stable xenon-enhanced computed tomography (developed by Gur et al. in Pittsburgh) in our dog model with hypothermia. We found that cerebral perfusion decreased more than oxygen uptake following arrest.

Mild Hypothermia (34 to 36° C)

In the early 1980s, IRRC medical student Brader promoted the idea of external head cooling for cerebral preservation (intra-arrest, intra-CPR cooling). Since head cooling lowered brain temperature very slowly, we did not pursue this research at the time. Then, in 1987, we examined factors that might explain the variable neurologic outcomes after the same "normothermic" cardiac arrests in several series of dog experiments. We discovered that only mild hypothermia (35 to 36° C) correlated with good outcomes when inadvertently present at the start of ventricular fibrillation.⁴ All this logically led to a study of mild hypothermia for cerebral preservation (intra-arrest) and resuscitation (postarrest).⁵

We used our most reproducible dog outcome model: 12.5 minutes of ventricular fibrillation (no flow), arrest at normothermia, reperfusion with brief bypass, and intensive care to 96 hours. In the cooled groups, the head and neck were immersed in ice water starting at 3 minutes of arrest. (This lowered brain temperature only 1° C over 10 minutes.) Then, reperfusion with brief bypass instantaneously brought core and brain temperature to 34° C, where it was sustained for one hour. Clinical and morphologic outcomes were significantly better in the cooled groups (see figure, page 2). Myocardial necrosis scores and arrhythmias were the same in both hypothermic and normothermic dogs.

In 1989, this research led to a study of mild resuscitative hypothermia in a clinically relevant CPR dog model.⁶ Again, a normothermic control group achieved significantly worse outcomes than the two cooled groups. The group



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with total body surface cooling induced immediately after the restoration of spontaneous circulation had the same improved outcome as the other cooled group with additional external head cooling started with CPR. Another study of dogs is now in progress. In it, we are trying to dissect protective versus preservative versus resuscitative cooling at the mild versus moderate versus deep levels. We are also working on brain cooling methods. In all these studies even the dogs that achieved functional normality showed some histologic brain damage.

Comments

Also in 1988 to 1990, three other research groups (Ginsberg's group in Miami, Welch's in Detroit, and Siesjö's in Lund, Sweden) published data from cat and rat models of global brain ischemia (not cardiac arrest). These studies indicated that mild to moderate postcooling saved hippocampal neurons. There are data by others that suggest benefits from resuscitative hypothermia after brain trauma or focal ischemia. In our rat hemorrhagic shock model, survival times and rates were increased with hypothermia.⁷

Since mild cerebral hypothermia is safe and may benefit the insulted brain, I consider it ready for clinical development, while laboratory research is continued.

Anesthetized or critically ill patients may benefit from untreated mild hypothermia, provided shivering is prevented. Although external head and neck cooling can be started along with CPR, its effect is very slow; therefore, other cooling methods will have to be added. In cases of stroke or head injury, more time would be available for cooling. While mild brain cooling appears to be promising, I do not believe that it is a breakthrough in itself. It should, however, become part of a mechanism-specific combination treatment protocol for cardiac arrest cases, which we are now developing.

The mechanism of hypothermia-induced protection, preservation, or resuscitation is not clear.

Reduced cerebral oxygen consumption alone cannot explain these effects. We postulate a synergism of several physicochemical mechanisms. Considering the complexity of the postresuscitation syndrome and its therapeutic prevention or mitigation, not only the victims, but also the investigators, should keep their heads cool.

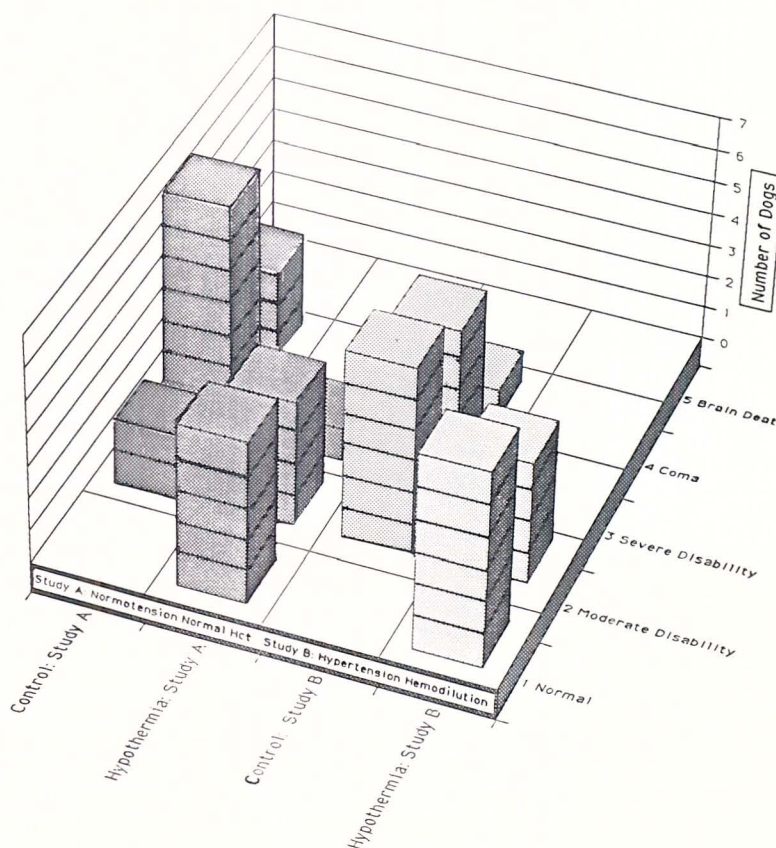
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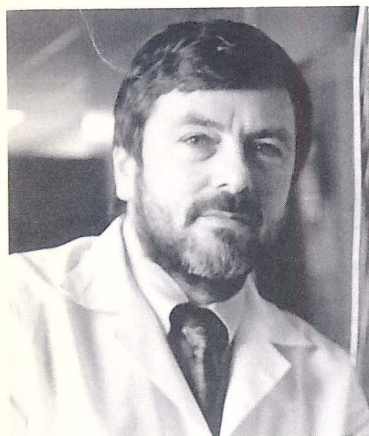
- 1Bigelow. *Ann Surg* 132:849, 1950;
- 2Gisvold, et al. *Stroke* 15:803, 1984;
- 3Leonov, et al. *Anesthesiology* 69:A845, 1988; 4Safar, et al. *Am J Emerg Med* 8:55, 1990; *Crit Care Med* 16:923, 1988; 5Leonov, et al. *J Cereb Blood Flow Metab* 10:55, 1990; 6Sterz, et al. *Crit Care Med* 18:S222, 1990;
- 7Crippen, et al. *Ann Emerg Med* 17:407, 1988.

Best overall performance category (OPC) at 24-96h after cardiac arrest of 12.5 min in dogs. Best OPC 1 or 2, "good outcome"; best OPC 3, 4, or 5, "poor outcome." The only hypothermic dog with poor outcome (OPC 3 in Hypothermia Study A) had severe arrhythmias and worse myocardial necroses than the others.

**Study A: $p < 0.01$ OPC 1 vs. 2-5; $p < 0.001$ OPC 1-2 vs. 3-5
Study B: $p < 0.01$ OPC 1 vs. 2-5; $p < 0.05$ OPC 1-2 vs. 3-5**

Leonov, et al: *J Cereb Blood Flow Metab* 10:57, 1990





Michael Pinsky, M.D., new editor of the *Journal of Critical Care*

Pinsky Named Editor

Michael Pinsky, M.D., is the new editor of the *Journal of Critical Care*. The journal, inaugurated in 1986, has gained a reputation for reporting excellent scientific work in the field of intensive care medicine. Several other faculty members have recently been appointed to editorial positions. Our group of editors and board members now includes: Charles W. Buffington, M.D., Associate Editor, Anesthesiology; Editorial Board Member, *Journal of Cardiothoracic Anesthesia*; Bradley P. Fuhrman, M.D., Editorial Board Member, *Critical Care Medicine*, *Critical Care Outlook*, and *Journal of Pediatrics*; Patrick M. Kochanek, M.D., Editorial Board Member, *Stroke*; Etsuro K. Motoyama, M.D., Editorial Board Member, *Pediatric Pulmonology*; Michael R. Pinsky, M.D., Editor, *Journal of Critical Care*; Editorial Board Member, *Applied Cardiopulmonary Pathophysiology*, *Chest*, and *Critical Care Medicine*; Thomas E. Rudy, Ph.D., Editorial Board Member, *Cognitive Therapy and Research*; Peter Safar, M.D., Editorial Board Member, *Resuscitation*; and Peter M. Water, M.D., Editorial Board Member, *Critical Care Medicine*.

Research Retreat Hosted

Where should department research be headed in the 1990s? Some sixty faculty members began to forge the answers to this key question at the department's recent research retreat, organized by Dr. Leonard Firestone, Vice-Chairman for Research.

On February 2 and 3 at the Oakland Holiday Inn, the department's various clinical teams and laboratories presented research summaries. Such diverse sites as the Cardiopulmonary Physiology and Children's Hospital laboratories, the Anesthesiology core facility, the IRRC, and the Pain Evaluation and Treatment Institute were represented. Included in the program were panel discussions of research planning issues such as productivity and funding in research and the future of research training programs.

An overriding theme emerged: Creating new knowledge is a vitally important priority and is the mutual responsibility of faculty members and the department leadership. Many felt that the department should continue to build on traditional strengths, for example, in cardiopulmonary physiology and at the same time promote further development in the multidisciplinary neurosciences. It was also concluded, however, that although organ-oriented physiology and pathophysiology have served anesthesiology well over several decades, the new emphasis in the department on molecular and cellular biology and pathogenesis is appropriate, timely, and important. Given the recent expansion in departmental research staff and facilities, Dr. Firestone predicted that we are very well positioned to meet the creative challenges ahead.



David Wilks, M.D., Director of Residency Program

A Good Match

The department had a highly successful match this year, gaining 13 fine residents from a high quality national pool of applicants. Joining our department at the Clinical Base Year level are: Richard Kuntz, Medical College of Wisconsin; Steven Levin, University of Pittsburgh; Janet Wilczak, Wayne State University; David Rust, University of West Virginia; Lois Lamp, University of Michigan; Sanjay Chaudhry, SUNY-Syracuse; and Frederick Ganzi, University of Michigan.

Joining us in July 1991, at the CA-1 level will be: Carole Fetzer, Tulane University; Martin Asinari, UMDNJ; Elizabeth Schaidler, University of Oklahoma; Shi Jei Wu, University of Pittsburgh; David Johnson, Penn State University; and John Lindenthal, Texas Tech University. It is particularly exciting to be welcoming these fine trainees to our department.

ACGME Accredits Residency

Last June the residency program was reviewed by Herman Turndorf, M.D., representing the Accreditation Council for Graduate Medical Education. Reviewing an institution of our size and diversity (70,000 anesthetics per year; 127 faculty; 70 residents) is certainly no simple assignment. Dr. Turndorf spent two days talking to staff physicians, residents, and hospital administrators and studying voluminous supporting materials. The outcome, announced in October, was full four-year accreditation of the anesthesiology residency.

Acute Pain Rotations Offered at PUH

In the past year the department has developed Acute and Cancer Pain Services at Presbyterian-University Hospital. Residents are now offered one-month rotations on these services, directed by Drs. Michael Brody, David Burke, and Charles Richards. The rotations cover assessment and management of acute postsurgical pain, acute non-surgery-related pain, and cancer-related pain.

For acute pain management, residents are taught techniques of patient-controlled analgesia, continuous opioid infusion, oral opioid analgesia, epidural and intrathecal opioid use, and psychological modalities.

On the Cancer Pain Service residents learn to assess and manage diverse cancer-related pain syndromes as part of a multidisciplinary team. They gain experience in the use of oral opioids and non-opioid adjuvants such as anticonvulsants and tricyclic antidepressants. Additional modalities include epidural and intrathecal opioids, nerve blocks, including neurolytic procedures, and psychological techniques.

These rotations also provide didactic teaching during daily clinical rounds as well as formal teaching rounds. Residents are expected to become familiar with selected pain literature. These busy clinical services offer valuable experience in the anesthesiologist's role as a consultant outside of the operating room.

In Memoriam



Charles W. Schertz, M.D. 1954-1990

An Anesthesiology Research Fellowship has been established in memory of our colleague Charlie Schertz, who died in an avalanche March 27, 1990, while attempting to climb Mount Manaslu in north-central Nepal. A memorial service was held April 17 at St. Paul's Cathedral, and a reception followed. The family has requested that any memorial contributions be sent to the University Anesthesiology/CCM Foundation, marked, "For the Dr. Charles W. Schertz Anesthesiology Research Fellowship."

Nursing Update



Dennis Stroup,
MSN, CRNA,
Codirector,
Anesthesia
Nursing Program

Stroup New Codirector of Anesthesia Nursing

We welcome Dennis Stroup, MSN, CRNA, who joined the University of Pittsburgh Anesthesia Nursing Program as Codirector in January. Mr. Stroup was Director of the Phase II US Army Program in Anesthesia Nursing at William Beaumont Army Medical Center in El Paso, Texas.

Mr. Stroup brings extensive experience in nurse anesthesia education and practice. He has held faculty appointments at Texas Wesleyan University and at SUNY-Buffalo.

Among Mr. Stroup's activities in Anesthesia Nursing will be teaching, clinical supervision, and graduate student advisement on thesis committees and alternative research requirements.

Student Research Assistants Available

Graduate students in the Anesthesia Nursing Program must complete a thesis or alternative research requirement for the master's degree. For the alternative research requirement, the student may develop a project or research question related to a faculty research program. Data already collected by faculty may be used. Faculty members engaged in research who would like to have an anesthesia graduate student assist them should contact Dennis Stroup at 624-4722. Research ideas are welcome and will be communicated to incoming students.

As Others See Us

Pittsburgh's Good Fortune

A recent issue of Money Magazine has rated Pittsburgh among the ten best cities for business. Pittsburgh ranked sixth this year in the Fortune 500 rating, based on annual sales figures for corporations headquartered in the city.

Could Pittsburgh be a place that makes New Yorkers, Chicagoans, and San Franciscans envious? Architecture critic Brendan Gill, writing in the *The New Yorker*, said this: "Indeed, the ideal population of a city today is about that of Pittsburgh, and the ideal area of a city is—again like that of Pittsburgh, which is fifty-five square miles—comparatively small." Gill goes on, "What a New Yorker especially responds to in Pittsburgh is a sense of the city as an organism whose many parts have been made to function as they were designed to. The note struck in Pittsburgh is not one of hysteria but one of equilibrium." Twice in the past five years, the *Places Rated Almanac* named Pittsburgh "Most Liveable City"; it's been in the top five all five years.

Pittsburgh's reputation has catapulted to the top in just ten years. While the decline of the historic steel industry has certainly brought sadness, endeavors establishing Pittsburgh as a noted center for corporate business and medical and engineering research

"The note struck in Pittsburgh is not one of hysteria but one of equilibrium"

have renewed the face of the city. The skyline is studded with new buildings incorporating modern functional design and materials in a way that complements and enhances our historical architectural inheritance. The city's stunning panorama at the exit from the Fort Pitt Tunnel says it all: Pittsburgh is thriving.



Left to Right: Mr. David Tkach, Administrative Director; Dr. Etsuro Motoyama, Vice-Chairman and Vice-Chairman for Clinical Affairs;

Dr. Leonard Firestone, Vice-Chairman for Research; Dr. Richard Stiller, Director of the Anesthesiology/CCM Research Laboratories



A New Publication

It is a pleasure to announce the birth of a new vehicle of communication for the Department of Anesthesiology and Critical Care Medicine and its faculty, trainees, alumni, and friends. With the proliferation of journals, newsletters, and assorted throwaways, it seems to me that any new publication needs to justify its existence. The intent of this one is to provide a forum in which various aspects of departmental activities are made accessible—whether these activities concern research matters, changes in departmental governance, evolutions in clinical and teaching programs, or simply congratulations for accomplishments.

Were we a small department, such an endeavor would probably be unnecessary and perhaps even pretentious. The reality, however, is that we

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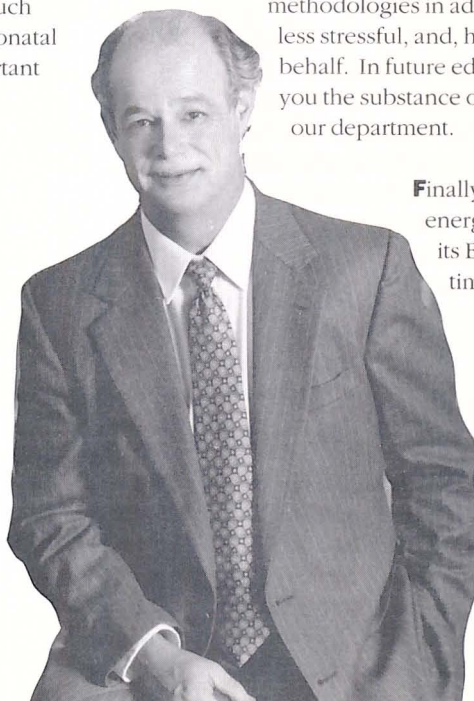
everyone is informed

about relevant events"

are such a large group that I can no longer assume that everyone is informed about relevant events. Comparisons with other academic anesthesia departments (based on survey data from the Society of Academic Anesthesia Chairmen) now begin to be possible for the first time and are very helpful. Some of the conclusions we knew all along, while others were unexpected.

We are the largest academic anesthesia department in the United States, with 127 faculty (the average is 29) and more than 100 trainees. We are also among the most productive. We are among the top 20% in external research funding. (Available data don't tell us where in the top 20%.) We are among the top 5% in research productivity, as judged by the number of peer-reviewed papers published. Although gratifying, self-congratulation is not the point. Rather, the point is that it is no longer possible for the members of the department, not to mention its alumni, to keep informed by word-of-mouth and such tribal councils as faculty meetings. I hope that this neonatal publication will fill, at least in part, that real and important need.

Peter M. Winter, M.D.,
Chairman,
Department of Anesthesiology
and Critical Care Medicine



New Positions

Integral to the question of size and communication is that of governance. As the department's mass, output, programs, and finances have grown, we have, to a greater or lesser extent, outgrown the methodologies by which we got here. The department has approximately tripled since 1979, and its budgets have increased by more than a factor of four. The longer I have been chairman, the more I have learned to depend on the wisdom of colleagues. Whether that is maturation on my part, or maturation on the part of the department's faculty, I have yet to sort out. For this and other reasons, major administrative changes have taken place within the last year, and I wish to describe them briefly.

In August, **Mr. David Tkach**, who is a CPA and holds an MBA in health care management, was hired as our Administrative Director. Mr. Tkach had previously held major administrative positions at Eye & Ear Hospital and at Presbyterian-University Hospital. During the eight months he has been here, he has already made a very positive impact.

Dr. Steven Finestone, who had been Vice-Chairman and Vice-Chairman for Clinical Affairs since 1979, has stepped down from that position and will remain Chief of Anesthesiology at Montefiore Hospital. **Dr. Etsuro Motoyama**, who had been Vice-Chairman for Research since 1979, has taken the role of Vice-Chairman and Vice-Chairman for Clinical Affairs. **Dr. Leonard Firestone** has been named Vice-Chairman for Research. **Dr. Robert Willenkin**, currently on sabbatical leave in England, will remain Vice-Chairman for Academic (Teaching) Affairs. **Dr. Richard Stiller, Ph.D.**, an analytical chemist, has joined the department and will be director of the core laboratory facilities. **Dr. Edwin Nemoto**, who has faithfully filled that position for 15 years, will return to a full-time research role.

The three vice-chairmen, Mr. Tkach, Dr. Ryan Cook, Dr. Jan Smith, and I meet on a monthly basis to discuss a wide range of issues important to the department. The combination of changes in responsibility and new methodologies in administration has made my job more interesting, less stressful, and, hopefully, more productive on the department's behalf. In future editions of this newsletter I will try to share with you the substance of these changes and their practical outcomes for our department.

Finally, I wish to thank **Dr. Helena Gunnerson** for the energy and creativity she has put into this newsletter as its Editor, and **Ms. Lisa Cohn**, our department's long-time Scientific Editor, for her help in its production.



Research Seed Grants Awarded

In January results of the biannual seed grant competition were announced. Grants were awarded to: Nicholas Bircher, M.D., for "Effect of Sodium Bicarbonate on Cardiac Resuscitation and Neurological Outcome"; Charles Buffington, M.D., for "Isoflurane and Collapse of Flexible Stenosis"; Richard Coyle, M.D., for "Does Alpha-2 Receptor Agonism Inhibit the Development of Neurogenic Pulmonary Edema?"; and Daniel Pickle, M.D., for "Mechanism of Improved Survival When Isoproterenol Is Used to Treat Bupivacaine-induced Cardiac Arrest."

Other current grant-holders, who received awards in July, are: Luke Chelluri, M.D., for "The Pharmacokinetics of Lidocaine and Monoethylglycinexylide Following Orthotopic Liver Transplantation"; Leonard Firestone, M.D., for "Does the Benzodiazepine Inverse Agonist Ro15-4513 Increase the Anesthetic Requirement by a Specific or a Functional Mechanism?"; Isao Kusakawa, M.D., for "Incorporation of 3H-thymidine by Airway Smooth Muscle Cells in a Rat Model Exposed to Chronic Normobaric Hypoxia"; Marshall Millman, M.D., Ph.D., for "Lipid Analysis of Skeletal Muscle Triads Isolated from Malignant-hyperthermia-susceptible Pigs"; Joseph Quinlan, M.D., for "Effects of General Anesthetics on the

Benzodiazepine Receptor"; Paul Rogers, M.D., for "Hyperinflation and Patterns of Breathing During Weaning from Synchronized Intermittent Mandatory Ventilation versus Pressure Support Ventilation"; and Robert Schlichtig, M.D., for "Hierarchy of Blood Flow Redistribution and Critical Oxygen Delivery of Brain and Other Organs During Endotoxic/Hemorrhagic Shock."

Annual Outing Moves to Beechwood Farms

Mark your calendars for the annual Resident/Advisor Outing, to be held this year at Beechwood Farms Nature Reserve on Saturday, August 11, 1 to 8 PM.

Beechwood Farms offers lush foliage, hiking trails, and ample space for quiet reflection or a rousing game of softball. Traditional Pittsburgh picnic fare will be served, rain or shine!

Alumni Reception at ASA

The department will host a reception for faculty and alumni at the 1990 ASA Annual Meeting. Please be our guests at the Mirage Hotel in Las Vegas on Sunday, October 21, from 6 to 8 PM.

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